

## REMARKS

Upon entry of this amendment, claims 1-7 and 55-83 are pending. The amendments to claim 1 are supported in the specification, for example, at paragraphs [0020] and [0067]. New claims 84-89 are supported in the specification, for example, at paragraphs [0031] and [0032]. New claim 90 is supported in the specification, for example, at paragraph [0050]. New claim 91 is supported in the specification, for example, at paragraph [0049].

### Obviousness-Type Double Patenting Rejection

Reconsideration is respectfully requested of the rejection of claims 55-65 and 68 as being unpatentable over claims 1 and 6-7 of U.S. Patent No. 6,709,744 (the '744 patent). The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.<sup>1</sup> However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.<sup>2</sup>

Claim 1 of the '744 patent follows.

What is claimed is:

1. A bioactive material having the formula



wherein x is from about 20% to about 35%;

y is from about 20% to about 35%;

z is from about 0% to about 10%; and

q is from about 30% to about 50%.

In contrast, current claim 55 has these express requirements:

- (1) a regular or irregular particle of hydroxyapatite
- (2) prepared from molded water-soluble glass containing about 1-40 wt.% of a calcium component, about 5-65 wt.% of an alkali metal oxide component and about 20-94 wt.% of a glass former,
- (3) other than glass containing 20-35 wt% CaO, 20-35 wt.% Na<sub>2</sub>O, 0-10 wt.% P<sub>2</sub>O<sub>5</sub> and 30-50 wt.% B<sub>2</sub>O<sub>3</sub>,

<sup>1</sup> *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991).

<sup>2</sup> *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

(4) transformed in a phosphate solution at a temperature of less than about 100°C, and

(5) the hydroxyapatite particle having substantially the same shape as the molded water-soluble glass.

Claim 1 of the '744 patent does not teach or make obvious instant claim 55 because claim 55 requires that the glass be other than glass containing 20-35 wt% CaO, 20-35 wt.% Na<sub>2</sub>O, 0-10 wt.% P<sub>2</sub>O<sub>5</sub> and 30-50 wt.% B<sub>2</sub>O<sub>3</sub>. This requirement excludes the bioactive glass that is the subject of claim 1 of the '744 patent. Further, the '744 patent does not teach or provide a reason for one skilled in the art to deviate from the formulation of '744 claim 1 and instead formulate a glass according current claim 55. Thus, claims 55-65 and 68 are patentable over claims 1 and 6-7 of the '744 patent.

### **35 U.S.C. § 102 Rejection**

Reconsideration is respectfully requested of the rejection of claims 1, 3-4, 55-65, and 67 as being anticipated by Brown (WO96/29144).

#### Claim 1

Claim 1 is directed to a calcium phosphate agglomerate which has these express requirements:

- a) the agglomerate is a product of an agglomeration formed as an agglomeration of water-soluble glass bodies transforms into an agglomeration of calcium phosphate bodies, and
- b) the agglomerate has a shape and size that are substantially the same as that of the agglomeration of the plurality of water-soluble glass bodies from which the agglomerate is formed.

The critical nature of the water-solubility and transformation aspects of (a) are explained in the specification:

[0019] In general, the calcium phosphate bodies of the present invention are derived from a water-soluble glass body containing calcium. When the glass is immersed in or otherwise contacted with an aqueous phosphate solution, the

glass dissolves, thereby releasing  $\text{Ca}^{2+}$  ions into the aqueous phosphate solution. In this solution,  $\text{Ca}^{2+}$  ions react with  $\text{PO}_4^{3-}$  and  $\text{OH}^-$  ions to form calcium phosphate which has a relatively low solubility limit in the aqueous phosphate solution. As the dissolution of the glass proceeds, the concentration of calcium phosphate increases in the solution until the solubility limit of calcium phosphate is exceeded and, as a consequence, calcium phosphate is deposited as a porous calcium phosphate layer on the outer surface of the water-soluble glass body. The formation of this porous calcium phosphate layer on the water-soluble glass body, however, does not prevent further dissolution of the water-soluble glass. Rather, the glass continues to dissolve and, as it does, the thickness of the porous calcium phosphate layer increases. Eventually, the water-soluble glass is completely dissolved, leaving only a porous calcium phosphate body.

Brown describes hydroxyapatite compositions prepared from a particulate agglomerate composition and a polymeric material for bone substitutes. Brown specifically explains that his particulate agglomerate compositions are prepared by

mixing (i)  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$  particles with (ii) particles of a calcium source comprising  $\text{Ca}_4(\text{PO}_4)_2\text{O}$ , in a non-aqueous liquid wherein said  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$  and said calcium source comprising  $\text{Ca}_4(\text{PO}_4)_2\text{O}$  are present in an amount sufficient to form phase-pure hydroxyapatite having a Ca/P ratio of 1.5 to 1.67, to form said particulate agglomerates.<sup>3</sup>

Upon contact with an aqueous solution that, in some embodiments, contains phosphate ions, hydroxyapatite (a special form of calcium phosphate) is formed.<sup>4</sup>

Stated another way, applicants' claim is a product formed from a starting material of water-soluble glass bodies in an agglomeration. This agglomeration of water-soluble glass bodies is transformed into a calcium phosphate agglomeration. In contrast, Brown starts with calcium phosphate particles and a) forms an agglomeration of calcium phosphate powder particles in a non-aqueous solution, and then b) contacts these intimately mixed particles in an aqueous solution to form hydroxyapatite (a form of calcium phosphate). Brown makes an agglomeration of *calcium phosphate bodies* in (a), and *never* has an agglomeration of *water-soluble glass bodies*. So Brown necessarily cannot have applicants' required "product of an agglomeration [from] an agglomeration of a plurality of water-soluble glass bodies." And it follows, necessarily, that Brown cannot have applicants' required "calcium phosphate agglomerate having a shape that is substantially the same as that of *the agglomeration of the*

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<sup>3</sup> See WO 96/29144 at page 9.

<sup>4</sup> See id. at page 23.

*plurality of water-soluble glass bodies,"* in view of the glaring absence of water-soluble glass bodies from Brown's process. These are express requirements that cannot be ignored in assessing patentability. Additionally, new claims 58-65 are dependent from claim 1, incorporate all the requirements of claim 1, and are patentable for similar reasons as claim 1. Thus, claims 1, 3-4, and 58-65 are not anticipated by the Brown reference.

#### Claim 55

Claim 55 is described above in connection with the obviousness-type double patenting rejection. The Brown reference is described above and does not disclose calcium phosphate bodies prepared by transforming molded water-soluble glass particles. Because the Brown reference does not describe or use molded water-soluble glass in the transformation, the particles produced in the Brown reference cannot have substantially the same shape as the molded water-soluble glass used in the transformation. Thus, claims 55-57 and the claims that depend therefrom are not anticipated by the Brown reference.

### **35 U.S.C. § 103 Rejections**

#### *1. Claims 1-7 and 67 over Day et al.*

Reconsideration is respectfully requested of the rejection of claims 1-7 and 67 as being unpatentable over Day et al. (U.S. Patent No. 6,358,531) under 35 U.S.C. § 103. Day et al. disclose calcium phosphate *spheres* prepared from alkali borate glass microspheres or irregular particles having a size from about 5 microns to about 1000 microns.<sup>5</sup>

#### Claim 1

In contrast to Day et al.'s spheres, claim 1 requires an *agglomerate* of a plurality of calcium phosphate bodies, and that this agglomerate has the same shape as bonded-together water-soluble glass particles prior to transformation (as amended). The Office asserts that no particular shape is required by claims 1 and 55. But this is not the case because claims 1 and 55 require an agglomerate of glass particles that are transformed into an agglomerate of phosphate bodies having substantially the same shape as the agglomerate of glass particles. And as amended, claim 1 underscores that the agglomerate of glass particles is a plurality of individual particles bonded together. The specification describes the agglomerates as follows:

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<sup>5</sup> See U.S. Patent No. 6,358,531 at column 6, lines 7-11.

The shape and size of the agglomerates of calcium phosphate bodies are dependent on the number of water-soluble glass bodies to be transformed into calcium phosphate bodies, the shape and size of the reaction vessel and the degree of agitation of the phosphate solution while the transformation process is occurring.<sup>6</sup>

Thus, the product of claim 1 is "a body" which is a product of "*a plurality of* bodies." See, for example, in [0049]: "In one embodiment the agglomerate contains at least about 10 calcium phosphate bodies." This is consistent with the definition of "an agglomerate": particles "clustered or growing together, but not coherent."<sup>7</sup> Moreover, claim 1 has been amended to underscore the fact that "the agglomeration of the plurality of water-soluble glass bodies is individual particles of the water-soluble glass bonded together."

In contrast, to a plurality of water-soluble glass particles bonded together, the products of the cited Day et al. disclosure are *discrete* particles. For example, the description of Figures 7, 8, and 9 refers to shells, concentric shell, and porous, homogeneous gels. This description does not describe an agglomerate that has individual glass particles "bonded together" as required by claim 1. Moreover, Figures 4, 7, 8 and 9 show discrete microspheres, and not an agglomerate of phosphate bodies. Thus, the Day et al. reference does not disclose all the elements of claim 1 and would not have provided a reason for a person skilled in the art to prepare an agglomerate of phosphate bodies as claimed in claim 1. The Day reference would not have provided a reason for a person skilled in the art to prepare an agglomerate of bonded-together water-soluble glass bodies for transformation to an agglomerate of calcium phosphate bodies because the only embodiments contemplated therein are individual microspheres or irregular glass particles.<sup>8</sup> Thus, claim 1, and the claims that depend therefrom are patentable over the Day et al. reference.

Further, claim 2 depends from claim 1, requires all the elements of claim 1 and further requires the agglomerate to contain at least about 10 calcium phosphate bodies. Thus, this agglomerate starts with at least 10 water-soluble glass particles bonded together and the resulting agglomerate of calcium phosphate bodies has substantially the same shape as the agglomerate of water-soluble glass particles. Moreover, the Day reference does not describe fused agglomerates of water-soluble glass bodies having at least 10 glass bodies that is transformed to the corresponding agglomerate of 10 calcium phosphate bodies having the same shape as the glass

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<sup>6</sup> See specification at paragraph [0049].

<sup>7</sup> Merriam-Webster's Collegiate Dictionary, 10th ed., 1993, Merriam-Webster, Inc., Springfield, Massachusetts.

<sup>8</sup> Of course these are shown in certain figures and described to be in groups or assemblages, but never as bonded-together agglomerates.

body agglomerate. Further, the Day reference would not have provided a reason for a skilled person to select agglomerates containing at least 10 water-soluble glass bodies from the universe of possible configurations and compositions of glass bodies known in the art. Thus, claim 2 is patentable over Day et al.

#### Claim 55

Claim 55 is directed to regular or irregular particles of hydroxyapatite prepared from molded water-soluble glass and has substantially the same shape as the molded water-soluble glass. Claim 55 is described in more detail above.

The Day reference is described above and does not disclose calcium phosphate bodies prepared by transforming molded water-soluble glass particles. Because the Day reference does not describe or use molded water-soluble glass in the transformation, the particles produced in the Day reference cannot have substantially the same shape as the molded water-soluble glass used in the transformation. Thus, the Day et al. reference does not disclose all the elements of claim 55 and would not have provided a reason for a person skilled in the art to prepare calcium phosphate bodies having substantially the same shape as the molded glass particles used in the transformation. Again, the Day reference would not have provided a reason for a person skilled in the art to prepare hydroxyapatite particles having substantially the same shape as the molded glass particle because the only embodiments disclosed in the Day reference were particles that were not molded. Thus, claim 55 and the claims that depend therefrom are patentable over the Day et al. reference.

#### *2. Claims 55-65 and 68-83 over Day et al. in view of Hayakawa et al.*

Reconsideration is respectfully requested of the rejection of claims 55-65 and 68-83 as being unpatentable over Day et al. in view of Hayakawa et al. (*J. Am. Ceramics Soc.* 1999:2155-2160) under 35 U.S.C. § 103. Claim 55 and the Day et al. reference are described above. Hayakawa et al. describe hydroxyapatite particles deposited on a sodium silicate glass. The hydroxyapatite is formed by soaking the alkali silicate glass in simulated body fluid that contains phosphate ions for several hours. The Office asserts that it would have been obvious "to form hydroxyapatite in the invention of Day et al."<sup>9</sup> However, Hayakawa does not remedy the deficiencies of the Day et al. reference. Hayakawa describes deposition of hydroxyapatite on the

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<sup>9</sup> See page 8 of the Office action dated January 23, 2009.

crushed particles of sodium silicate glass, but does not describe any shape of the resulting hydroxyapatite particles. Hayakawa et al. do not. Further, since the Hayakawa glass particles are crushed, a skilled person would not have had any reason to start with a molded glass particle to prepare the hydroxyapatite particles.

Moreover, claim 56 requires a glass former of B<sub>2</sub>O<sub>3</sub> (borate) and Hayakawa discloses only silicate glass formers. It would not have been obvious to a person of skill in the art that a borate glass would have had the same reactivity as the silicate glass of Hayakawa. Thus, it would not have been obvious to substitute the borate of claim 56 for the silicate of Hayakawa to prepare a hydroxyapatite product having a particular shape. In sum, claims 55-65 and 68-83 are patentable over Day et al. in view of Hayakawa et al.

3. *Claims 55 and 66 over Day et al. in view of Hayakawa et al. and Jin et al.*

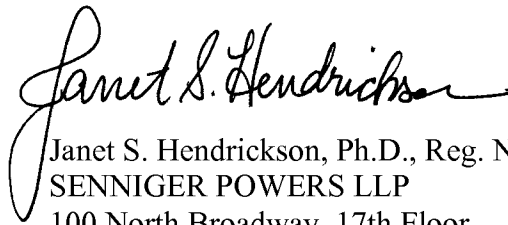
Reconsideration is respectfully requested of the rejection of claims 55 and 66 as being unpatentable over Day et al. in view of Hayakawa et al. (*J. Am. Ceramics Soc.* 1999:2155-2160) and Jin et al. (*J. Biomedical Materials Res.* 2000:491-499) under 35 U.S.C. § 103. Claim 55, the Day et al. reference, and Hayakawa et al. are described above. Jin et al. describe porous particles, blocks, and honey-comb-shaped particles of hydroxyapatite. These hydroxyapatite particles are prepared from a paste of hydroxyapatite powder that was shaped with a mechanical device. Thus, the Jin reference does not disclose hydroxyapatite particles prepared by transforming molded water-soluble glass particles. Because the Jin reference does not describe or use molded water-soluble glass in the transformation, the particles produced in the Jin reference cannot have substantially the same shape as the molded water-soluble glass used in the transformation. Thus, claims 55 and 66 are patentable over the cited references.

**CONCLUSION**

Applicant submits that the present application is in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

A handwritten signature in black ink, reading "Janet S. Hendrickson", with a stylized flourish at the end.

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